REMARKS

The Advisory Action states that the claim amendments in the Amendment dated February 28, 2007 will not be entered. Applicants respectfully submit and request entry of the present Amendment.

Upon entry of this Amendment, claims 1-13 and 15-26 are pending in the application. Claim 14 has been canceled. Claim 26 is new. Claims 13 and 25 have been amended. Support for claim 26 can be found in the specification, such as on page 20.

Referring to page 2 of the Advisory Action, the Examiner asserts that claim 25 raises a new issue under 35 U.S.C. § 112, second paragraph. The Examiner asserts that claim 25 depends from canceled claim 14.

Claim 25 has been amended to depend from claim 13.

Further, the Examiner asserts that the phrase "liposomes having an average diameter in the range of 100-1000 μm" in claim 13 raises issues of new matter.

Claim 13 presently recites that the liposomes have an average diameter in the range of 100-1000 nm.

The specification describes that vesicles may be relatively large or small. *See* pages 19-20. The specification also describes that the vesicles thereof preferably have a mean diameter not exceeding 500 nm, and preferably substantially all have diameters less than 2000 nm. As examples of a relatively large vesicle, the specification describes that the vesicle diameter may be "in the range of 300 nm to 5000 nm; preferably less than 2000 nm, preferably with average diameters in the range of 500-1000 nm." *Id.* As examples of the relatively small vesicle, the

specification describes that the vesicle diameter thereof may be "in the range of 100 nm to 400 nm preferably with average diameters in the range 200 to 300 nm." *Id.*

In view of these descriptions in the specification, a person skilled in the art would immediately appreciate that the specification supports an average diameter in the range of 100-1000 nm. *See* MPEP § 2163.05(III). The specification does not indicate that the example ranges of the relatively large size and relatively small size of the vesicles are mutually exclusive. To the contrary, the specification indicates that the examples ranges of the relatively large and small sizes are inclusive, as the example vesicle diameters of the relatively large vesicle (300 nm to 5000 nm) overlaps with the vesicle diameters of the relatively small vesicle (100 nm to 400 nm). The specification also describes that all vesicles thereof preferably substantially have diameters "less than 2000 nm." In this regard, a person skilled in the art would immediately appreciate that the example ranges described in the specification are examples of a broader range of from 100 nm to 1000 nm.

Further, a person skilled in the art would immediately appreciate the selection of 100 nm and 1000 nm from the example ranges described in the specification.

Therefore, the amendments to the claims add no new matter. Entry of the Amendment is respectfully submitted.

I. Claim Rejections - 35 U.S.C. § 112

Referring to the Office Action dated October 30, 2006, claims 13-16 and 25 have been rejected under 35 U.S.C. § 112, second paragraph.

Without admitting that this rejection is appropriate, Claim 13 has been amended to recite "a composition for the co-delivery to a cell of a nucleic acid and an assistor protein, wherein the nucleic acid operatively encodes an antigenic protein or portion thereof which shares at least one epitope with the assistor protein, the composition comprising said nucleic acid and said assistor protein associated with liposomes formed from liposome forming materials, the liposomes having an average diameter in the range of 100-1000 μm".

Applicants submit that the claims are now clear and withdrawal of this rejection is requested.

Claim 16 has been rejected under 35 U.S.C. § 112, first paragraph.

Applicants again traverse this rejection for the reasons set forth on pages 10-13 of the Amendment filed August 8, 2006. Additionally, without admitting that this rejection is appropriate, Claim 13 has been amended to recite the feature of now cancelled Claim 14. Specifically, Claim 13 now recites that the immune response comprises an antibody response specific to the antigenic protein and/or assistor protein. Accordingly, Applicants submit that the claims comply with the requirements of Section 112, first paragraph, and withdrawal of this rejection is requested.

II. Claim Rejections - 35 U.S.C. § 102

Claims 13-16 and 25 have been rejected under 35 U.S.C. § 102(b) as being anticipated by WO 97/28818 to Craig et al.

Applicants again respectfully traverse this rejection for the reasons set forth in the Amendment filed August 8, 2006. Additionally, Claim 13 has been amended to recite that the

average diameter of the liposomes is in the range of 100-1000 μm. Support for this amendment to Claim 13 is provided by page 20, line 4, for the minimum and page 20, line 3, for the maximum.

Craig mentions liposomes at page 12, line 23, but no details are given as to the nature of the liposomes.

Additionally, amended Claim 13 recites that the weight ratio of nucleic acid to protein is in the range of 1000:1 to 1:1. This range is not disclosed in Craig. Craig has some description of the relative amounts of nucleic acid and protein. At page 25, from line 29, there is reference to the "stoichiontric" ratio of the components in the mixture. From line 34 there is a definition of a ratio of nucleic acid to peptide. Presumably, this is the stoichimetric ratio mentioned earlier. However, reference to stoichiometric ratio is unusual, and unclear in the context of nucleic acid mixed with a polypeptide. The word stoichiometric is normally applied to starting materials which react together. However the nucleic acid and the polypeptide do not react together to form a covalent conjugate. Certainly "stoichiometric" is often used to distinguish from "weight" when referring to ratio of components. Accordingly, the ratios specifically mentioned on lines 36-38 of page 25 do not appear to be weight ratios.

The only other disclosure of the relative amounts of the nucleic acid and the protein seem to be in the worked examples. For instance on page 54, from line 32, a recipe is given for a complex which contains 437.5mg protein (NBC9) and 87.5mg DNA (pEGFP-N1). Thus the ratio of nucleic acid to protein is around 1:5. On page 56, lines 14-15, the ratio of plasmid

nucleic acid to protein is 1:2. At page 58, from line 30 to 33, 96mg protein is mixed with 28mg nucleic acid, giving a nucleic acid : protein ratio of around 1:3.4.

Thus the ratio of nucleic acid to protein is at least a factor of 2 outside the end of the range (1:1) defined in Claim 13. Applicants submit that a person skilled in the art would not be led to use a complex of nucleic acid and protein with the weight ratio within the range defined in Claim 13 of the present application based on the disclosure of Craig.

In view of the foregoing, withdrawal of this rejection is requested.

III. Claim Rejections - 35 U.S.C. § 103

Claims 13-16 and 25 have also been rejected under 35 U.S.C. § 103 as being unpatentable over U.S. Patent No. 6,166,177 to Probst et al. in view of Gregoriadis et al.

Applicants also respectfully traverse this rejection.

Probst describes vaccines for providing an immune response against chlamydia. At column 8, line 19 -27, a vaccine composition comprising polypeptide antigen is described. The polypeptide may be incorporated into a liposome, which acts as an adjuvant. At column 8, from line 28-51, there is a description of a gene vaccine, which is an alternative to the peptide vaccine described previously. There is no disclosure in this paragraph of liposomal delivery systems for gene vaccines.

The subsequent paragraph of Probst, from column 8, line 52-59, describes combination type vaccines. These involve simultaneous or sequential administration of a DNA vaccine with a polypeptide. At line 55-59, it is suggested that DNA maybe administered "in a delivery system as described above", but this is only in connection with a sequential system. Thus the nucleic

acid and the polypeptide must be separately formulated and administered, whether naked or in a delivery system.

There is no disclosure of a delivery system which is appropriate for both nucleic acid and polypeptide antigens. There is no disclosure of using a liposomal delivery system for a gene vaccine. There is no suggestion of using a single composition containing both gene vaccine and polypeptide. Even if the nucleic acid and polypeptide are to be administered simultaneously, it is not necessary and there is no specific suggestion that the two components must be present in a single composition.

The Examiner relies upon the Gregoriadis paper to show that it would be obvious to formulate the nucleic acid and the protein into liposomes. Gregoriadis discloses that proteins may be entrapped into liposomes. Gregoriadis also discloses that nucleic acid, specifically DNA vaccines may be entrapped into liposomes. However, Gregoriadis does not describe co-entrapment of more than one active into the same liposomes. Nor does Gregoriadis suggest entrapment of both protein and nucleic acid into the same liposomes.

There is nothing in Gregoriadis therefore that would lead a person skilled in the art to form liposomes containing both protein and nucleic acid vaccines in the same liposomes. There is nothing in Gregoriadis et al that would lead a person skilled in the art to expect any benefit by such co-entrapment. Nor is there any disclosure in either Probst et al or Gregoriadis et al which would lead to selection of the particular range for the weight ratio of nucleic acid protein specified in Claim 13.

The examples in the present specification show that there is a surprising benefit in the co-entrapment method defined in Claim 13 as compared to other ways of co-administering the peptide antigen a nucleic acid vaccine. For instance if the effect were merely to be protection of the ingredients and entrapped within the liposomes from the surrounding environment, an add mixture of separately entrapped protein and nucleic acid would be expected to have the same effect as the co-entrapped mixture. The data shown there is a surprising benefit in the co-entrapped mixture. The benefit is believed to be the result of both components being simultaneously delivered into antigen presenting cells, as explained in the passages mentioned previously, from page 12, line 19 onwards. Neither Probst, nor Gregoriadis would lead a person skilled in the art to expect these benefits.

For the above reasons the Applicant believes that the present invention is not obvious over a combination of the teachings of Probst et al with Gregoriadis et al.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

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